DETAILED ACTION

This application has been transferred from Molly Baughman to Cynthia Wilder of Art Unit 1637. Any future correspondence should be directed to Examiner Cynthia Wilder whose contact information appears at the end of this Office action.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-15 in the reply filed on 1/14/2008 is acknowledged. Accordingly, claims 16-19 are withdrawn from consideration as being drawn to a non elected invention.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1-9, 11, 14 and 15 rejected under 35 U.S.C. 103(a) as being unpatentable over by Nilsson et al {Nilsson I, herein) (Journal of Molecular recognition, vol. 10, page 7-17, 1997) in Nilsson et al {Nilsson II, herein} (WO 9609407, citation made or record in IDS filed 5/11/2007).

Regarding claim 1, Nilsson I teach a method for monitoring the amplification of a plurality of different target polynucleotides comprising carry out a reaction for the amplification of a plurality of different target polynucleotides, during the amplification reaction, contacting different amplified products with a molecule that binds to or interact with a polynucleotide, the molecule being located in a spatially defined position and detecting the interaction between the amplified products and the molecules by measuring changes in applied radiation (page 8-9).

Nilsson I does not teach wherein the amplification and detection process in carried out in a single reaction chamber.

Nilsson II teaches a similar to that of Nilsson I for monitoring the amplification of a target polynucleotide in a single reaction chamber, the method comprising carrying out a reaction for the amplification of a target polynucleotide, during the amplification reaction contacting the amplified product with a molecule that binds to or interact with a polynucleotide, the molecule being located in a spatially defined position or being determined by a non-linear or non-fluorescent technique and detecting the amplified product and the molecule by measuring changes in applied radiation (see pages 4, lines 23-26, page 6, lines 10-37 and pages 9-12). Nilsson II teaches that this process is

advantageous because it allows the possibilities of monitoring the actual progress of activities for quantifying a nucleic acid molecule (see pages 1-2).

On of ordinary skill in the art at the time of the claimed invention would have been motivated to have modified the nucleic acid quantification method of Nilsson I to encompass a single reaction chamber rather than multiple reaction vessels for the advantages of monitoring the actual progress of activities which takes place during the quantification of the nucleic acid as taught by Nilsson II. The instant claims are prima facie obvious over the teachings of Nilsson I and Nilsson II in the absence of secondary consideration.

Regarding claim 2, Nilsson I teaches wherein the molecule is immobilized to a support material (page 8-9).

Regarding claim 3, Nilsson II teaches wherein the method can be modified to encompass different reagents to enhance the signal during detection. These reagents include DNA polymerase enzyme, antibodies, or free nucleotides (page 12, lines 30-38).

Regarding claim 4, Nilsson I teaches wherein the molecule is a polynucleotide, at least a portion of which is complementary to a region on an amplified product (pages 8-9).

Regarding claim 5 and 6, Nilsson I teaches wherein the oligonucleotide or short nucleic acid sequences capable of use as a primer in amplification reaction or a probe in hybridization (see page 8 and 10).

Regarding claim 9, Nilsson I teaches wherein the detecting is carried out by measuring changes in Surface Plasmon Resonance (SPR) (page 8-9).

With regards to the claims 7-9, 11, and 14, these claims merely recite a plethora of conventional nucleic acid manipulation reagents and methodologies, as well as well as routine optimization or reaction components, concentrations, and parameters. Clearly such conventional and trivial modification and optimizations do not contribute towards patentability. For example, Nilsson et al teach a plurality of biosensor technologies which are known and used in the art (see entire reference, especially page 4, line 26-37 to page 5, lines 1-37). Thus, one of ordinary skill in the art would have been motivated to modify the primary references in the manner of the claims to achieve the expected benefits, optimizations and/or expanded applications. It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to carry out the claimed methods using any of the plethora of non-linear or non-fluorescent techniques associated with biosensor technologies known in the art.

Regarding claim 15, Nilsson II teaches wherein flow cells are used in the reaction. The references do not expressly teach that the reaction vessels are sealed. However, as noted in MPEP 2144.07, it is *prima facie* obvious to select a known process based on its suitability for the intended purpose. In this case, Nilsson I teaches the use of flow cells for performing the hybridization reaction and Nilsson II teaches the use of flow based sensor chips for carrying the coamplification and hybridization reaction. Given the teachings in both Nilsson I and Nilsson II, it would have been obvious to one of ordinary skill in the art to encompass flow cells that are sealed for maintaining and monitoring the reaction conditions. The claim is *prima facie* obvious in the absence of secondary consideration.

5. Claims 10, 12 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nilsson I in view of Nilsson II and further in view of Sun et al (20040161750, filing date 2/14/2003). Regarding claims 10, 12, and 13, Nilsson I and Nilsson II teach a method for monitoring an amplification reaction as previously discussed above. The references do not expressly teach wherein the molecule comprises a metallic particle or wherein the detection is carried out using an intercalating label that binds to form a hybrid or wherein the intercalating label is fluorescent.

Su et al provide a method similar to that of Nilsson I and Nilsson II for monitoring an amplification reaction, the method comprises carrying out a reaction for the amplification of a target polynucleotide in combination with detection via a non-linear or non-fluorescent technique (0034-0056). Su et al teach wherein the fluorescent tags are conjugated to the oligonucleotide probes (0034-0037). Su further teaches wherein in some cases nanoparticles such as gold or silver may be attached to the oligonucleotide probe array (0045, 0047). Su et al teach that the use of fluorescent label, including nanotags are advantageous for increase sensitivity and specification of detection of the target molecule (0007).

One of ordinary skill in the art at the time of the claimed invention would have been motivated to modify the nucleic acid quantification method of Nilsson I and Nilsson II to encompass fluorescent tags for the obvious benefit of increasing sensitivity and specificity of biomolecule detection as suggested by Su et al.

Conclusion

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CYNTHIA B. WILDER whose telephone number is (571)272-0791. The examiner can normally be reached on a flexible schedule.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cynthia B. Wilder/
Patent Examiner
Art Unit 1637

4/13/2008